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Economic Burden of Adult Pharyngitis: The Payer's Perspective

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ABSTRACT

Objectives: Although not recommended by practice guidelines, physicians frequently prescribe an antibiotic for adults with viral pharyngitis. The financial burden of this practice, from the payer's perspective, has not been previously evaluated. The purpose of this study was to estimate those expenditures.

Methods: A cost-of-illness study was performed to estimate annual expenditures of pharyngitis management from the payer's perspective. National Ambulatory Care Survey data were used to represent current patterns of ambulatory care visits and antibiotic prescriptions for adult pharyngitis. Direct and antibiotic resistance costs were summed to estimate total expenditures for pharyngitis management. Resistance costs were calculated using a model linking the effect of antibiotic consumption to the cost consequences of resistant *Streptococcus pneumoniae* infection. Sensitivity analyses compared cost outcomes of current practice, adherence to pharyngitis management guidelines from the Infectious Diseases Society of America (IDSA), and nonantibiotic treatment.

Results: In the base-case analysis, reflecting current practice patterns, total expenditures were $1.2 billion with antibiotic resistance contributing 36% ($426 million). IDSA guideline adherence decreased costs to $559 million with resistance accounting for 6.8% ($37.9 million). Guideline adherence plus reducing office visits by 30% decreased costs to $372 million, with only 1.4% ($5.3 million) due to resistance. Additional cost-savings of $88 million were realized by using a nonantibiotic treatment strategy.

Conclusions: Current practice imposed a substantial economic burden on the payer, while guideline adherence resulted in cost reductions, especially in terms of resistance, emphasizing that antibiotic prescribing habits have broad economic consequences. Relevant stakeholders, payers, physicians, and other health-care providers should revisit efforts to encourage adherence to pharyngitis guidelines to reduce health-care costs.

Keywords: adults, antibiotic resistance, cost-of-illness analysis, pharyngitis.

Introduction

More than 11 million patients annually with acute pharyngitis seek medical attention in the ambulatory care setting [1]. Like other upper respiratory infections (URI) in adults, pharyngitis is caused by a virus in 80% to 90% of cases [2]. Group A streptococci (GAS) is the only bacterial etiology of pharyngitis for which antibiotic treatment, usually with penicillin, is routinely recommended [2]. Accordingly, only 10% to 20% of adult patients should receive treatment with a recommended antibiotic. In contrast, ambulatory care physicians provided an antibiotic prescription from 47% to 73% of adults with pharyngitis [3–5]. Many were for nonrecommended, newer, and more expensive agents [4,5]. Excessive antibiotic use can contribute to the development of antibiotic resistance leading to the use of more expensive drugs and more costly outcomes from infections with resistant bacteria [6–8]. Annual expenditures related to antibiotic resistance in the United States were estimated to be at least $5 billion [9]. One study indicated that more than $1.1 billion was spent annually on unnecessary antibiotic prescriptions for adults with URI [10].

To help combat the overuse of antibiotics for URI, practice guidelines for adult pharyngitis have been circulated. The American College of Physicians recommends clinical indicators to identify adults with a high probability of GAS pharyngitis [11], while those from the Infectious Diseases Society of America (IDSA) are more stringent, because antibiotic treatment is recommended only for patients with clinical features of GAS pharyngitis plus a positive rapid antigen detection test (RADT) [12]. Nonetheless, 66% of physicians in a health-care plan failed to adhere to either one of these guidelines [3].

The cost consequences to the health-care payer of pharyngitis management are not known. A database examination of nearly 14,000 insured employees in 1997 found that acute pharyngitis cost the employer $30 million in health-care benefits, with outpatient expenditures estimated at $628 per beneficiary.

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Nevertheless, the authors did not mention whether a practice guideline was used to aid management decisions. In addition, they reported costs in broad categories without providing detailed information about the distribution of diagnostic and therapeutic expenditures [13]. Therefore, we undertook a cost-of-illness (COI) study to determine the payer's cost of pharyngitis management incurred by: 1) current practice patterns; 2) adherence to IDSA guidelines; and 3) no antibiotic treatment. A COI study measures the economic burden of a disease and highlights areas to target cost reductions [14–16].

Methods

Definition of Costs

The current COI study was prevalence-based from the payer's perspective with a time horizon of 1 year. We divided expenditures into direct and resistance costs. Direct costs were those associated with professional services, testing, antibiotic prescriptions, and antibiotic-induced drug rash and anaphylaxis. Resistance costs were those related to hospitalization with community-acquired pneumonia (CAP) caused by *Streptococcus pneumoniae* resistant to beta-lactam or macrolide antibiotics; referred to as drug-resistant *Streptococcus pneumoniae* (DRSP). Total costs were the sum of direct and resistance expenditures.

We used 2006 Medicare reimbursement rates to the authors' institution to represent unit prices for professional services, RADT, drug rash, and anaphylaxis (Table 1). Antibiotic treatment for pharyngitis was divided into recommended and nonrecommended agents. Penicillin and erythromycin were considered recommended antibiotics, while extended spectrum penicillins, cephalosporins, macrolides, and quinolones were considered nonrecommended [5]. The cost for a course of a recommended or nonrecommended antibiotic was determined by multiplying its wholesale price per dose by its suggested duration for GAS pharyngitis [12,17]. We then summed the treatment costs for all the recommended or nonrecommended antibiotics, and divided the result by the respective number of prescriptions for each group to arrive at the average treatment price for a course of a recommended or nonrecommended antibiotic (Table 1).

Table 1 Unit prices for direct costs

Category	Unit price ($)
Professional services for pharyngitis	68.00
RADT	17.00
Recommended antibiotic course	7.00
Nonrecommended antibiotic course	30.00
Drug rash	60.00
Anaphylaxis	13,922.00

RADT, rapid antigen diagnostic test.

Characteristics of Cohorts

We used data from the National Ambulatory Medical Care Survey (NAMCS) to create the characteristics of the NAMCS cohort [5]. The NAMCS is administered by the National Center for Health Statistics (NCHS) and Center for Disease Control and Prevention. Findings are based on a sample of patient visits to nonfederally funded office-based physicians who are primarily engaged in direct patient care. The NAMCS utilizes a multistage probability design which involves three stages in determining selection of patient visits: geographic location, physician specialty, and visits within annual practices of sampled physicians. Since 1989 the survey has been conducted annually. Data collection is completed by the staff at the sampled practices. Each visit is weighted by NCHS to allow extrapolation to national figures. We used summary data from an analysis of NAMCS data which was designed to evaluate antibiotic prescribing for adult pharyngitis visits during the period 1989 to 1999 [5]. In the NAMCS cohort (Table 2), the number of adults with pharyngitis seeking ambulatory care was set at 6.7 million [5]. Also reflecting NAMCS data, 73% (4.9 million) of patients received an antibiotic, with 78% (3.8 million) receiving a nonrecommended agent and 22% (1.1 million) receiving one that was recommended. We estimated that 80% (5.36 million) of 6.7 million patients would receive a RADT [3]. The rates of antibiotic-induced rash and anaphylaxis were set at 3% and 0.1%, respectively [18].

Sensitivity analyses of direct costs were done by varying key characteristics of the NAMCS cohort. In one analysis, we applied the IDSA practice guidelines to the NAMCS population of 6.7 million adults. We called this cohort IDSA-NAMCS (Table 2). In another analysis, we applied the guidelines to a reduced population of 4.7 million adults with pharyngitis, reflecting a 30% reduction in office visits for pharyngitis. We referred to this group as the IDSA-reduced population (IDSA-RP) (Table 2). The percentage of patients receiving a RADT was also varied to reflect adherence to guideline recommendations [3]. Two scenarios of no testing, no antibiotic treatment were also analyzed. The no-testing, no-treatment option applied to the NAMCS population was called NTX-NAMCS and its application to the reduced population of pharyngitis patients was the NTX-RP cohort (Table 2).

Calculation of Direct Costs

The estimated direct cost of each cohort characteristic was calculated as the product of its unit cost (Table 1) and frequency (Table 2). Total annual direct costs were then calculated. The direct expenditure per patient encounter was calculated for the NAMCS and IDSA-NAMCS groups, by dividing their total annual direct costs by their population size. It was not calculated for the reduced population cohorts (IDSA-RP and NTX-

Table 2 Characteristics of cohorts

Variable	NAMCS	IDSA-NAMCS	NTX-NAMCS	IDSA-RP	NTX-RP
Patients seeking medical care for pharyngitis	6.7 million	6.7 million	6.7 million	4.7 million	4.7 million
Patients receiving antibiotic therapy*	4.9 million (73%)	871,000 (13%)	0	611,000 (13%)	0
Patients receiving RADT*	5.36 million (80%)	2.7 million (41%)	0	1.9 million (41%)	0
Patients receiving recommended antibiotics†	1.1 million (22%)	871,000 (100%)	0	611,000 (100%)	0
Patients receiving nonrecommended antibiotics†	3.8 million (78%)	0	0	0	0
Antibiotic-related rash†	147,000 (3%)	26,130 (3%)	0	18,330 (3%)	0
Antibiotic-related anaphylaxis†	4,900 (0.1%)	871 (0.1%)	0	611 (0.1%)	0

*The number and percentage of pharyngitis patients in each cohort who received antibiotic therapy or a RADT.
†The number and percentage of antibiotic-receiving patients in each cohort who received a recommended or nonrecommended antibiotic, or experienced an antibiotic-related rash or anaphylaxis.
IDSA, Infectious Diseases Society of America; NAMCS, National Ambulatory Medical Care Survey; NTX, no treatment; RADT, rapid antigen diagnostic test; RP, reduced population.

RP), because they were created by proportional reductions of the IDSA-NAMCS and NTX-NAMCS cohorts. Therefore, patient expenditure per encounter would be similar to those groups.

Calculation of Resistance Costs

Antibiotic consumption at the population level is a recognized cause of DRSP [19–22]. Therefore, we estimated single-year costs resulting from DRSP CAP leading to hospitalization with full recovery. We did not include resistance expenditures attributable to development of newer and more expensive drugs, because they are not generally assumed by the payer [23].

Annual resistance costs were calculated using PΔV€, where P is the prevalence of DRSP in the community, ΔV, whose components are shown in Table 3, represents the likelihood of hospitalization with DRSP CAP multiplied by its cost, and € represents the proportional effect of antibiotic use on resistance [24]; that is, when antibiotic use for pharyngitis is intense, we assumed that € = 1, moderate € = 0.5, and low € = 0.1. Therefore, € reflects the elasticity of the effects of antibiotic use on resistance rates. One would expect respective resistance rates to increase or decrease during periods of intense or reduced antibiotic use [24]. In the primary analysis of resistance expenditures in the NAMCS group, we arbitrarily set € at 1 to reflect the high level of antibiotic use in this group. In the antibiotic-sparing IDSA-NAMCS and IDSA-RP cohorts, resistance rates should be lower, reflecting less intense use of antibiotics. In these groups, € was arbitrarily set at 0.5 or 0.1, respectively.

To calculate the cost effects of resistance (PΔV €), we placed P at 0.20, reflecting a reasonable estimate of DRSP in the United States [25,26]. To determine ΔV for hospitalization with DRSP CAP, we calculated the product of its likelihood multiplied by its cost as shown in Table 3. The product of P and ΔV was then multiplied by the different values of €, reflecting differences in the intensities of antibiotic use. Therefore, we studied the impacts of the different treatment strategies on the price of antibiotic resistance. As noted previously, in the primary analyses of resistance costs € was assessed at three levels: € = 1, correlated with the NAMCS cohort; € = 0.5, correlated with the IDSA-NAMCS cohort; and € = 0.1, correlated with the IDSA-RP cohort. In secondary analyses, we tested assumptions made about €. For the NAMCS cohort, we evaluated a range of € from 0.8 to 1; for the IDSA-NAMCS cohort a range of € from 0.3 to 0.7 was tested; and for the IDSA-RP cohort € was tested at values of 0.1 and 0.2. Aggregate resistance expenditures were calculated as the product of resistance costs from a single antibiotic course and the annual number of antibiotic prescriptions. The contribution of resis-

Table 3 Components used to calculate ΔV (cost consequence of DRSP)

Nonmonetary components of ΔV	Frequency	Reference
Annual adult episodes of CAP	4 million	[46]
A. Patients hospitalized	0.15 (600,000)	[46]
B. Hospitalizations with *S. pneumoniae**	0.50 (300,000)	[46,47]
C. Hospitalized patients with DRSP†	0.20 (60,000)	[25,26]
Monetary components of ΔV	Unit price ($)	NA
D. Single hospitalization with DRSP‡	29,000	NA
Calculation of ΔV	(0.15)(0.50)(0.20)(29,000)	[24]
ΔV ($)	435	NA

*Based on epidemiological data indicating that about 50% of episodes of CAP are caused by *S. pneumoniae*.
†Based on data indicating that at least 20% of *S. pneumoniae* isolates would be DRSP.
‡Additional Medicare reimbursement to authors' institution for hospitalization with drug resistant CAP.
CAP, community-acquired pneumonia; DRSP, drug-resistant *Streptococcus pneumonia*; NA, not applicable.

Table 4 Total direct costs ($) associated with each cohort analysis*

Variable	NAMCS	IDSA-NAMCS	NTX-NAMCS	IDSA-RP	NTX-RP
Office visits	455 million	455 million	455 million	320 million	320 million
RADT	91 million	46 million	0	32 million	0
Recommended antibiotics	8 million	7 million	0	4 million	0
Nonrecommended antibiotics	114 million	0	0	0	0
Antibiotic-related rash	9 million	2 million	0	1 million	0
Antibiotic-related anaphylaxis	68 million	12 million	0	9 million	0
Total direct costs	745 million	522 million	455 million	366 million	320 million

*Costs in millions.
IDSA, Infectious Diseases Society of America; NAMCS, National Ambulatory Medical Care Survey; NTX, no treatment; RADT, rapid antigen diagnostic test; RP, reduced population.

tance to the price of each patient encounter was calculated as the difference of the total cost and direct cost divided by the cohort size.

Results

Total Direct Costs

In the analysis of the NAMCS cohort, total direct expenditure for 1 year was $745 million ($111 per patient encounter), with antibiotic treatment-related costs (RADT, prescriptions, adverse reactions) accounting for 39% ($290 million) and professional fees accounting for 61% ($455 million). Antibiotic prescriptions for nonrecommended agents comprised 93% of total prescription costs (Table 4). Implementation of the IDSA guidelines to the NAMCS population (IDSA-NAMCS) resulted in total direct costs of $522 million ($78 per patient encounter), a 30% reduction. In this scenario, costs related to antibiotic treatment comprised 13% of the total with professional fees accounting for the remainder. Because only recommended antibiotics were used, prescription costs were reduced by 95% ($115 million) (Table 4). Evaluation of the IDSA-RP group resulted in total direct costs of $366 million, with antibiotic prescriptions accounting for 1.1%. Applying the no-testing, no-treatment option to the NAMCS population (NTX-NAMCS) would result in an annual direct cost of $455 million ($68 per patient encounter), reflecting a 39% ($290 million) reduction over the NAMCS group and a 13% ($67 million) reduction over the IDSA-NAMCS group. Finally, the direct costs of a no-treatment option applied to the population of 4.7 million adults with pharyngitis (NTX-RP) would be $320 million, decreasing costs by 58% over the NAMCS cohort, 39% over the IDSA-NAMCS cohort, and 12% over the IDSA-RP cohort (Table 4).

Resistance Costs

In the primary analyses of resistance expenditures, we assumed intense antibiotic use in the NAMCS cohort and set € = 1. The estimated price of resistance, calculated as the resistance cost for a single antibiotic course multiplied by the total number of prescriptions, was $426 million. For the IDSA-NAMCS and IDSA-RP primary analyses, we placed € at 0.5 and 0.1 to reflect reduced antibiotic use for pharyngitis. Resistance costs were $37.9 million and $5.3 million, respectively (Table 5). Thus, the no-antibiotic-treatment option would save an additional $5.3 million compared to IDSA-RP.

Because the value of € in the primary analyses was arbitrary, based on the assumed level of antibiotic use in each cohort, we conducted secondary analyses of each group by using various levels of €. In the NAMCS cohort, resistance costs could range from $326 million (€ = 0.8) to $426 million (€ = 1). In the IDSA-NAMCS cohort resistance costs spanned from $22.7 million (€ = 0.3) to $53 million (€ = 0.7). Resistance costs for the IDSA-RP cohort ranged from $5.3 million (€ = 0.1) to $10.6 million (€ = 0.2).

Total Costs

Annual total costs, calculated by adding direct and resistance costs, are shown in Figure 1. Resistance costs in these calculations were derived from the primary analyses of resistance expenditures, as described previously. In the NAMCS cohort, total costs were $1.2 billion ($179 per patient encounter), while in the IDSA-NAMCS group they were $560 million ($84 per patient encounter), a 48% reduction.

Table 5 Resistance costs associated with antibiotic use for pharyngitis

€, proportional effect of antibiotic use on microbial resistance*	1.0	0.5	0.1
Resistance costs per single course of antibiotics ($)†	87	43.50	8.70
Number of patients receiving antibiotic therapy‡	4,900,000	871,000	611,000
Aggregate resistance costs ($ millions)§	426	37.9	5.3

*Proportional effects of varied rates of antibiotic use on resistance. Three levels of € were evaluated: € = 1.0 corresponds to intense antibiotic use (NAMCS cohort); € = 0.5 corresponds to moderate antibiotic use (IDSA-NAMCS cohort); and € = 0.1 corresponds to limited antibiotic use (IDSA-RP cohort).
†Resistance costs were calculated as the product of PΔV and € as described in the Methods section.
‡The number of patients receiving antibiotic therapy in each analysis.
§Aggregate resistance costs are the product of resistance costs for a single course of antibiotic and the number of patients receiving antibiotic therapy for the respective level of €.

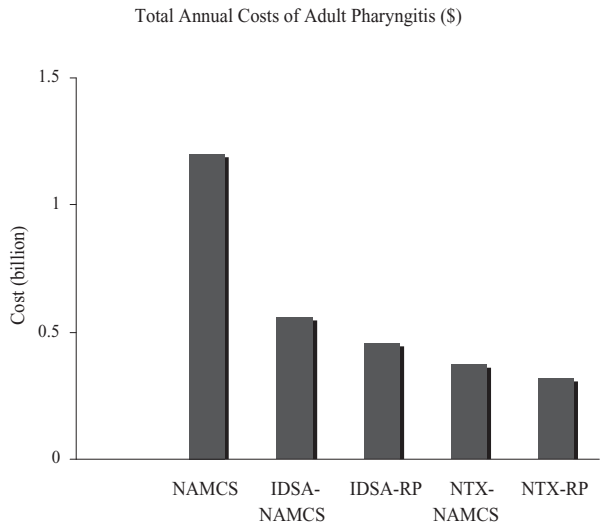

Figure 1 Total costs (direct and resistance costs) associated with each cohort analyzed. IDSA, Infectious Diseases Society of America; NAMCS, National Ambulatory Medical Care Survey; NTX, no treatment; RP, reduced population.

Thus, antibiotic resistance increased the cost of a patient encounter in the NAMCS cohort by 61% ($68), over the direct cost. Resistance added an additional 8% ($6) to the total cost per patient encounter in the IDSA-NAMCS group. Reducing physician visits by 30% and applying the IDSA guidelines (IDSA-RP) resulted in total costs of $372 million ($79 per patient encounter), reflecting a cost reduction from decreased resistance expenditures of 6% ($5) per patient encounter, compared to the IDSA-NAMCS cohort. Moreover, it represented a 44% ($100) per patient cost reduction due to decreased resistance expenditures compared to the NAMCS cohort. As noted previously, the NTX-RP option would result in $320 million in health-care costs, all attributable to professional services, reflecting a 16% decrease in total expenditures compared to the IDSA-reduced population analysis.

Discussion

Expert guidelines recommend antibiotic treatment of pharyngitis only for adults presenting with either clinical [11] or clinical plus microbiological evidence of GAS infection [12]. Contrary to this recommendation, many physicians continue to prescribe antibiotics to patients with a low probability of GAS [3]. Our COI study showed that this practice could cost health payers $1.2 billion annually in terms of direct expenditures and those associated with the development of antibiotic resistance. A unique finding of our work was that antibiotic resistance may increase health-care costs by 61% for each patient encounter. Several methodological issues must be considered when interpreting our conclusions.

The first was the use of the NAMCS data to estimate office visits and prescribing patterns for adult pharyngitis. This survey spanned the years of 1989 to 1999, and reported information only from nonfederally funded office practices in the United States [5]. Although these data were collected during the previous decade, they are the most recent longitudinal national information about adult pharyngitis available. Because the NAMCS reflects only information from nonfederally funded office practices, it would underestimate frequencies of office visits and antibiotic prescriptions for pharyngitis. In addition, we used Medicare reimbursement rates to assign costs, which may not provide an accurate reflection of the price of health care. If anything, we likely undervalued expenditures associated with pharyngitis management. Consistent with this notion, the mean payment for office visit costs was $315 for claims filed by an employed population with pharyngitis or tonsillitis [13].

The second issue is the type of economic analysis used. While a COI analysis highlights the economic impact of a disease or its prevention, it does not provide cost-effectiveness or cost-benefit information [16]. Quality-of-life measures are often omitted from COI studies because of the difficulty accurately quantifying them in monetary terms [16]. A related issue is that we did not include all costs associated with pharyngitis. We decided a priori to omit some direct costs, such as those associated with transportation, complications of GAS pharyngitis, and lost time from work. Complications of GAS pharyngitis, such as acute rheumatic fever (ARF) or peritonsillar abscess, were omitted because they are rare in adult patients, and there were no significant differences in their rates with or without antibiotic therapy [27–30]. Howie et al. reported that the risk of ARF in children (around 1:40,000) was similar regardless of whether antibiotic therapy was administered [31]. This risk would be even lower in adults, because ARF is mainly a disease of school-age children [30]. Finally, because antibiotic treatment does not speed return to work [28,32,33], lost time from work would be similar for all pharyngitis patients. These omitted expenditures would have little or no impact on the conclusions of our study.

The third issue is the validity of the mathematical model to measure antibiotic resistance costs. Although resistance to both GAS and *S. pneumoniae* have both been linked to antibiotic consumption at the population level [19–22,34,35], we estimated resistance costs generated by DRSP because its consequences have been defined better than those of resistant GAS [7]. The cost of resistance model quantitatively incorporates economic principles of resistance by linking its prevalence and cost consequences to different levels of antibiotic use [24]. Its characteristics gave us the ability to determine incremental cost changes at various intensities of antibiotic use. We showed that

resistance costs, as measured by hospitalization with DRSP, varied proportionately with antibiotic consumption, emphasizing the sensitivity of the relationship between consumption and resistance [21,36]. Our results probably underestimated the true cost of resistance to the payer because we did not include other expenditures such as death from resistant bacteria, nor resistance developing in other bacteria. Nonetheless, the preciseness of the results depends on how close the relationship between antibiotic consumption and the cost consequences of resistance approximates reality [24]. Mathematical models rely on data based on assumptions that have some degree of uncertainty, and more studies using complex modeling to determine resistance costs are clearly needed [36,37]. In the meantime, the importance of our findings was that the intensity of antibiotic use could be related proportionately to resistance expenditures, a concept supported by the work of others [24,36,37].

How can the results of our study be used by health-care payers? This COI analysis highlights the areas of antibiotic use and professional fees to target cost reductions. Expenses in both areas could be curtailed by development and implementation of educational programs for clinicians that convey the epidemiology and natural history of pharyngitis in otherwise healthy adults, and the cost consequences of antibiotic resistance. Excessive office visits and antibiotic use for pharyngitis stem from difficulties distinguishing GAS infection from viral etiologies [2], physician and patient overestimations of the consequences of untreated GAS pharyngitis [27,29,38], and physicians' expectations that patients want an antibiotic [39,40]. Contrary to physicians' beliefs, most patients with URI do not want an antibiotic [39]. Rather they seek reassurance and education from their physician [39]. Other investigators reported that patients who received an antibiotic for pharyngitis were 25% more likely to return to medical care for the same condition [41,42]. Physicians must understand that providing unnecessary antibiotic prescriptions promotes the patient's belief that an antibiotic is required for treatment, leading to excessive office visits, requests for antibiotic prescriptions, and higher costs.

Physicians must also understand how their individual prescribing habits contribute to health-care expenditures [24,43]. Relatively small cost consequences of resistance from a single antibiotic course for pharyngitis can become quite large when applied to all antibiotic courses for pharyngitis especially during periods of intense antibiotic consumption. This unrecognized outcome is rarely considered by physicians [23,24,43]. A literature review found that multifaceted educational programs were successful at reducing antibiotic prescribing [44]. Educational interventions conducted in France reduced colonization rates with resistant *S. pneumoniae* [21].

Finally, our study demonstrated that no antibiotic treatment dominated other treatment strategies. Although we did not measure health outcomes associated with no antibiotic treatment, routine antibiotic treatment of GAS may not be required [27,29,30]. A recent health outcomes study also found that foregoing testing and treatment in children with pharyngitis had both the lowest morbidity rate and costs from the payer's perspective [45]. Outcomes from no antibiotic treatment of GAS pharyngitis await better delineation. In the meantime, our study emphasized that better adherence to IDSA guidelines was associated with substantial cost-savings to the health-care payer.

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References

1 Schappert SM, Burt CW. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency rooms: United States, 2001–2002. National Center for Health Statistics. Vital Health Stat 2006;13:1–66.
2 Bisno AL. Primary care: acute pharyngitis. N Engl J Med 2001;344:205–11.
3 Linder JA, Chan J, Bates DW. Evaluation and treatment of pharyngitis in primary care practice. Arch Intern Med 2006;166:1374–9.
4 Ladd E. The use of antibiotics for viral upper respiratory tract infections: an analysis of nurse practitioner and physician prescribing practices in ambulatory care, 1997–2001. J Am Acad Nurse Pract 2005;17:416–24.
5 Linder JA, Stafford RS. Antibiotic treatment of adults with sore throat by community care physicians. A national survey, 1989–1999. JAMA 2001;286: 1181–6.
6 Howard DH, Scott RD II. The economic burden of drug resistance. Clin Infect Dis 2005;41(Suppl.): S283–6.
7 Tleyjeh IM, Tlaygeh HM, Hejal R, et al. The impact of penicillin resistance on short-term mortality in hospitalized adults with pneumococcal pneumonia: a systematic review and meta-analysis. Clin Infect Dis 2006;42:788–97.
8 Rubin RJ, Harrington CA, Poon A, et al. The economic impact of *Staphylococcus aureus* infection in New York City Hospitals. Emerg Infect Dis 1999;5:9–17.
9 Institute of Medicine. Antimicrobial Resistance: Issues and Options. Workshop Report. Washington, DC: National Academy Press, 1998.
10 Fendrick AM, Monto AS, Nightengale B, Sarnes M. The economic burden of non-influenza-related viral respiratory tract infections in the United States. Arch Intern Med 2003;163:487–94.
11 Snow V, Mottur-Pilson C, Cooper RJ, Hoffman JR. Principles of appropriate antibiotic use for acute pharyngitis in adults. Ann Intern Med 2001;134:506–8.

12 Bisno AL, Gerber MA, Gwaltney JM Jr, et al. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis. Clin Infect Dis 2002;35:113–25.
13 Birnbaum HG, Morley M, Greenberg PE, Colice GL. Economic burden of respiratory infections in an employed population. Chest 2002;122:603–11.
14 Rice DP. Cost-of-illness studies: fact or fiction? Lancet 1994;344:1519–20.
15 Byford S, Torgerson DJ, Raftery J. Cost of illness studies. Br Med J 2000;320:1335.
16 Segel JE. Cost-of-illness studies: a primer. 2006. Available from: http://www.rti.org/pubs/COI_Primer.pdf [Accessed March 1, 2007].
17 Drug Topics Red Book. Montvale, NJ: Thomson Healthcare, 2006.
18 Salkind AR, Cuddy PG, Foxworth JW. Is this patient allergic to penicillin? An evidence-based analysis of the likelihood of penicillin allergy. JAMA 2000;285: 2498–505.
19 Harbath S, Albrich W, Brun-Buisson C. Outpatient antibiotic use and prevalence of antibiotic-resistant pneumococci in France and Germany: a sociocultural perspective. Emerg Infect Dis 2002;12:1460–7.
20 Kristinsson KG. Effect of antimicrobial use and other risk factors on antimicrobial resistance in pneumococci. Microb Drug Resist 1997;3:117–23.
21 Guillemot D, Varon E, Bernède C, et al. Reduction of antibiotic use in the community reduces the rate of colonization with penicillin-G nonsusceptible *Streptococcus pneumoniae*. Clin Infect Dis 2005;41: 930–8.
22 Lipsitch M. Measuring and interpreting associations between antibiotic use and penicillin resistance in *Streptococcus pneumoniae*. Clin Infect Dis 2001;32: 1044–54.
23 McGowan JE Jr. Economic impact of antimicrobial resistance. Emer Infect Dis 2001;7:286–92.
24 Phelps CE. Bug/drug resistance. Sometimes less is more. Med Care 1989;27:194–203.
25 Hoban D, Waites K, Felmingham D. Antimicrobial susceptibility of community-acquired respiratory tract pathogens in North America in 1999–2000: findings of the PROTEKT surveillance study. Diagn Microbiol Infect Dis 2003;45:251–9.
26 Jacobs MR, Felmingham D, Appelbaum PC, et al. The Alexander Project 1998–2000: susceptibility of pathogens isolated from community-acquired respiratory tract infection to commonly used antimicrobial agents. J Antimicrob Chemother 2003;52:229–46.
27 De Meyere M, Mervielde Y, Verschraegen G, Bogaert M. Effect of penicillin on the clinical course of streptococcal pharyngitis in general practice. Eur J Clin Pharmacol 1992;43:581–5.
28 Dagnelie CF, Van der Graaf Y, De Melker RA. Do patients with sore throat benefit from penicillin? A randomized double-blind placebo-controlled clinical trial with penicillin V in general practice. Br J General Pract 1996;46:589–93.
29 Howe RW, Millar MR, Coast J, et al. A randomized controlled trial of antibiotics on symptom resolution in patients presenting to their general practitioner with a sore throat. Br J Gen Pract 1997;47:280–4.
30 Gordis L. The virtual disappearance of rheumatic fever in the United States: lessons in the rise and fall of disease. T. Duckett Jones Memorial Lecture. Circulation 1985;72:1155–62.
31 Howie JGR, Foggo BA. Antibiotics, sore throats and rheumatic fever. J R Coll Gen Pract 1985;35:223–4.
32 Zwart S, Sachs APE, Ruijs GJHM, et al. Penicillin for acute sore throat: randomised double blind trial of seven days versus three days or placebo in adults. Br Med J 2000;320:150–4.
33 Middleton DB, D'Amico F, Merenstein JH. Standardized symptomatic treatment versus penicillin as initial therapy for streptococcal pharyngitis. J Pediatr 1988;113:1089–94.
34 Seppälä H, Klaukka T, Vuopio-Varkila J, et al. The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A streptococci in Finland. N Engl J Med 1997;337: 441–6.
35 Martin JM, Green M, Barbadora KA, Wald ER. Erythromycin-resistant group A streptococci in schoolchildren in Pittsburgh. N Engl J Med 2004;346:1200–6.
36 Austin DJ, Kristinsson KG, Anderson RM. The relationship between the volume of antimicrobial consumption in human communities and the frequency of resistance. Proc Natl Acad Sci USA 1999;96:1152–6.
37 Levin BR, Lipsitch M, Perrot V, et al. The population genetics of antibiotic resistance. Clin Infect Dis 1997;24(Suppl.):S9–16.
38 Boxerbaum B. Prevention of streptococcal neurosis. Prim Care 1981;8:583–91.
39 Butler CC, Rollnick S, Pill R, et al. Understanding the culture of prescribing: qualitative study of general practitoners' and patients' perceptions of antibiotics for sore throats. Br Med J 1998;317:637–42.
40 Cowan PF. Patient satisfaction with an office visit for the common cold. J Fam Pract 1987;24:412–13.
41 Little P, Williamson I, Warner C, et al. Open randomized trial of prescribing strategies in managing sore throat. Br Med J 1997;314:722–7.
42 Little P, Gould C, Williamson I, et al. Reattendance and complications in a randomised trial of prescribing strategies for sore throat: medicalising effect of prescribing antibiotics. Br Med J 1997;315:350–2.
43 McGowan JE Jr. Minimizing antimicrobial resistance: the key role of the infectious diseases physician. Clin Infect Dis 2004;38:939–42.
44 Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database Syst Rev 2006;4:CD 003539.
45 Van Howe RS, Kusnier LP, II. Diagnosis and management of pharyngitis in a pediatric population based on cost-effectiveness and projected health outcomes. Pediatrics 2006;117:609–19.
46 Bartlett JG, Mundy LM. Community-acquired pneumonia. N Engl J Med 1995;333:1618–24
47 Musher DM, Spindel SJ. Community-acquired pneumonia. Curr Top Infect Dis 1996;16:102–24.